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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
NELSON, B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/28/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/869,386	Applicant(s) Sastry, et al.
	Examiner Brett Nelson	Group Art Unit 1648

☒ Responsive to communication(s) filed on *Sep 20, 1999* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *29-45, 47, and 49* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *29-45, 47, and 49* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

2. The examiner acknowledges receipt of the amendment filed Sep. 20, 1999 canceling claim 46, amending claim 29, and adding new claim 49. Claims under consideration are 29-45, 47, and 49. The examiner also acknowledges receipt of the Arlinghaus Declaration.

3. The rejection of claim 29, 31, 32, 41, and 45 rejected under 35 U.S.C. 102(e) as being anticipated by Berzofsky et al. (U.S. Pat. No. 5,820,865) is withdrawn in view of the amendments to the claims.

4. The rejection of claims 30, 33-40, and 42-44 under 35 U.S.C. 103(a) as being unpatentable over Berzofsky et al. in view of Haynes et al. (U.S. Pat. No. 5,013,548) is withdrawn in view of the amendments to the claims.

5. Claim 47 is objected to because it depends from claim 46 which was canceled. Appropriate correction is required. Claim 47 will be examined as if it depends from claim 29.

6. The objection to the application because of alterations which have not been initialed and/or dated as is required by 37 CFR 1.52(c) is maintained.

A properly executed oath or declaration which complies with 37 CFR 1.67(a) and identifies the application by application number and filing date is required.

7. The preliminary amendment filed Oct. 10, 1997, paper no. 6, is acknowledge, but was entered only in part. The amendments to the claims as well as the sequence listing were entered. However, the amendments to the specification were too numerous and were not entered.

A substitute specification excluding claims is required pursuant to 37 CFR 1.125(b).

If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

8. Applicant's arguments filed Sep. 20, 1999 have been fully considered but they are not persuasive.

9. The rejection of claims 29-45 and 47 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting HIV entry into a cell *in vitro* comprising contacting the cell with peptides consisting of SEQ ID NOs: 1, 3, or 5, does not reasonably provide enablement for a method of inhibiting HIV entry into a cell *in vivo* employing all of the possible claimed peptide sequences is maintained for reasons of record.

The rejection stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are drawn to a method of directly inhibiting HIV entry into a cell comprising contacting the cell with a composition comprising a peptide of 8-24 residues comprising SEQ ID NO:5. The specification at pages 65-67 and Fig. No. 8 disclose culturing MT-4 cells and primary human T cells in the presence of HIV and a selected peptide from the V3 loop of gp120 and the reverse transcriptase assays showed a decrease in the amount

of reverse transcriptase produced in the cells incubated with certain peptides. However, the specification does not show a correlation between that which occurred *in vitro* to that which one of skill in the art would reasonably expect *in vivo*.

The specification provides no probative evidence to support the claimed treatment which would protect humans against HIV infection. The obstacles to treatment development and therapeutic approaches with regard to retroviruses associated with AIDS in humans are well documented in the literature. These obstacles include: 1) the extensive genomic diversity associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to "hide" in the central nervous system where blood cells and neutralizing agents carried by the blood cannot reach the retrovirus, due to the blood-brain barrier and 5) the complexity and variation of the elaboration of the disease. The existence of these obstacles establish that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any vaccine or any immunization treatment or any therapeutic regimen on its face. In order to enable claims to drugs and their uses, either in vivo or in vitro data, or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the claims are sufficiently enabled. When the claims are directed to humans adequate animal data would be acceptable in those instances wherein one of ordinary skill in the art would accept the correlation to humans. Thus in order to rely on animal data there must exist an art-recognized animal model for testing purposes. See In re Hartop, 311 F.2d 249, 135 USPQ 419 (CCPA 1962).

Yarchoan et al. (J. Enz. Inh., 1992) state that while a number of agents have been found to block HIV binding to the target cell in vitro, these agents have generally not shown clear-cut evidence of clinical activity (abstract). Moreover, Gait et al. (TIBTECH 1995) discuss the problems associated with protein therapies for HIV and state that they suffer from problems of short serum half-life, poor bioavailability, and rapid clearance. Gait et al. also teach that as these problems were overcome, other problems emerged such as sequestration of the drug by serum proteins, drug resistance, and uneven distribution throughout the body, and that since these types of problems are unpredictable, it remains necessary to take into account the pharmacological parameters (p. 437).

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986)and reiterated by the Court of Appeals in In re Wands, 8 USPQ 2d 1400 at 1404 (CAFC 1988). In the instant specification, it is determined that: 1) there are no working examples which suggest the desired results of inhibiting HIV infection *in vivo*, 2) the nature of the invention involved the

complex and incompletely understood area of immunity to HIV, 3) the state of the prior art shows that prior treatment methods have been largely ineffective for the intended purpose, 4) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level), and 5) the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by prior failures. In view of all of the above, it is determined that the specification is not commensurate in scope with the claimed invention.

Applicant mainly urges that they have presented data which employ both *in vitro* and *in vivo* models via declaration, the results from the chimpanzee studies show that the claimed peptide inhibits HIV replication both in vivo and in vitro in chimpanzees, the ability if the claimed peptides to inhibit HIV infection has not been effectively challenged, applicants do not claim a cure for HIV but a method of inhibiting the progression of the disease, and Nehete et al. disclose the peptides from the V3 loop of HIV inhibit infection.

While applicant urges that they do not claim a cure for HIV but a method of inhibiting the progression of the disease, it is the examiner's position the claims recite a method for directly inhibiting HIV entry into a cell in a human subject. The claims do not appear to recite a method of inhibiting the progression of the disease, but can be broadly interpreted to read on a method of protecting a human from HIV infection. The Arlinghaus declaration states that the peptides inhibit HIV replication *in vitro* or in chimpanzees which is not the same as directly inhibiting HIV infection. Therefore, the declaration is not commensurate in scope with the claimed invention. Regarding the use of chimpanzees as models for HIV, Haynes (Science 1993) states that "in spite of an extraordinary amount of work in search of an animal model for human AIDS , no animal model exactly mirrors HIV infection". Haynes also states that the immune correlates of animal models to human regarding AIDS are not known (p. 1280 1st. col. 1st and 2nd. para.s) . Haynes, et al. (Ann. Med., 1996 p. 40) teach that major scientific obstacles blocking the development of successful HIV treatments are the extraordinary variability of HIV, the lack of an exact animal

model of HIV-induced AIDS, and the lack of understanding of the correlates of protective immunity to HIV (p 1280). It is clear that one of skill in the art at the time of applicant's invention would not have expected data employing chimpanzees to correlate to humans. It should be noted that the two Haynes references were cited in response to applicant's arguments regarding chimpanzees as models for HIV infection and do not constitute a new grounds of rejection. The Nehete manuscript employs *in vitro* data and is not commensurate in scope with the claimed invention.

Additionally, as previously stated, Yarchoan et al. (J. Enz. Inh., 1992) state that while a number of agents have been found to block HIV binding to the target cell in vitro, these agents have generally not shown clear-cut evidence of clinical activity (abstract). Moreover, Gait et al. (TIBTECH 1995) discuss the problems associated with protein therapies for HIV and state that they suffer from problems of short serum half-life, poor bioavailability, and rapid clearance. Gait et al. also teach that as these problems were overcome, other problems emerged such as sequestration of the drug by serum proteins, drug resistance, and uneven distribution throughout the body, and that since these types of problems are unpredictable, it remains necessary to take into account the pharmacological parameters (p. 437).

New Grounds of Rejection

Claim Rejections - 35 USC § 102

10. Claim 49 is rejected under 35 U.S.C. 102(e) as being anticipated by Berzofsky et al. (U.S. Pat. No. 5,820,865). The claims are drawn to a method for directly inhibiting HIV entry into a cell *in vitro* comprising contacting the cell with a peptide comprising a specific sequence. It should be noted that the phrase "for directly inhibiting HIV entry into a cell" is viewed as an intended and is given little patentable weight. Berzofsky et al. disclose a method for protecting cells from HIV comprising contacting cells *in vitro* with a composition that comprises a peptide having the claimed sequence (cols. 3-4). The method of Berzofsky et al. is the same as the claimed method. Therefore, Berzofsky et al. anticipate the invention as claimed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brett Nelson, Art Unit 1648 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1648 FAX telephone number is (703)308-4426. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Brett Nelson whose telephone number is (703) 306-3219.

If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

NELSON/bn BN
September 27, 1999

JEFFREY STUCKER
PRIMARY EXAMINER